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LIQUOR FERRI IODIDI.

By George M. Beringer, A.M., Ph.M.

The use of the Solution of Iron Iodide for the extemporaneous preparation of the Syrup is undoubtedly increasing. The dispensing doctors and the druggists who are either "too busy" or "too lazy" to make Syrup of Iron Iodide by the official process have willingly relegated to the manufacturer the preparation of the concentrated Solution of Ferrous Iodide, and have thus curtailed their own practice of the art of pharmacy to the simple admixture of such a concentrated solution with Syrup.

As long ago as 1888, this custom was sufficiently in vogue to be recognized by the National Formulary, and, in the first issue of that work in that year, a formula for Liquor Ferri Iodidi was included. The note accompanying that formula stated: "On mixing 1 volume of this Solution of Iodide of Iron with 5 volumes of Syrup, the product will contain about 60 grains of Iodide of Iron (ferrous) in each fluidounce, and will be practically, measure for measure, but not weight for weight, identical with the official Syrup of Iodide of Iron."

It will be thus seen that the extemporaneous preparation of syrup of ferrous iodide in this way had, even at that time, the endorsement of a quasi legal authority.

In the Third Edition of the N. F. published in 1906, the formula has been retained. In the earlier copies of this edition the foot-note stated: "This solution contains about *85* per cent. of Ferrous Iodide. On mixing 1 volume with *15 volumes* of Syrup (U. S. P.), the product will be practically identical with Syrup of Ferrous Iodide (U. S. P.)." Subsequently, this wording was changed, and in the later copies the note reads: "This solution contains about *81* per cent. of Ferrous Iodide. On mixing 1 volume with *11 volumes* of Syrup (U. S. P.), the product will be practically identical with Syrup of Ferrous Iodide (U. S. P.)."

As a matter of fact, both of these statements are incorrect. The N. F. III formula is directed to yield 1000 Cc. of product; if this be changed and the finished product made 1000 Gm. then the solution will contain 81 per cent. of Ferrous Iodide.

The manufacturers have quite generally adopted for the Solution of Ferrous Iodide a strength of sixteen times by volume that of the official Syrup of Iron Iodide. That is, their labels direct that to prepare Syrup Iron Iodide, 1 fluidounce of the Liquor be mixed with 15 fluidounces of Syrup. This is only another evidence that the American physicians, druggists and manufacturers persist in using the apothecaries' measure and think in its terms rather than in the decimal terms of the metric measure. The intent of the National Formulary evidently was to supply a formula for a preparation of the same strength as supplied in the trade.

Several other minor defects in the N. F. formula should be considered. The direction to filter the *boiling solution* of ferrous iodide through paper is a manipulative error that brings trouble. In my experience, hot solutions of ferrous iodide of the strength directed invariably eat right through paper filters, even if of several thicknesses. Either the solution has to be diluted greatly or cooled before filtering through paper or else the hot solution must be filtered through glass wool or asbestos wool, returning the first portion of the filtrate until it comes through clear.

The amount of Hypophosphorous Acid directed to be used in the formula is not the equivalent of that directed as a preservative in the official formula for the Syrup. Consequently, the Solution is prone to undergo change if kept in bottles that are opened frequently, as is apt to be the case. Hence, the Solution should be preserved in small glass stoppered bottles, which should be completely filled and kept tightly stoppered.

The proposition has now been made that the U. S. P. IX should direct that Syrup of Ferrous Iodide be prepared from a concentrated liquor, and, consequently, a formula for a concentrated Solution of Ferrous Iodide will have to be adopted as a new admission in the Pharmacopœia. Our concern is, that the most satisfactory formula be adopted.

The value of Glycerin as a preservative for solutions of iron salts has long been recognized by the practical pharmacists and the manufacturers of the various solutions of ferrous salts. As early as 1857, J. C. Leaming (Proceedings, American Pharmaceutical

Association), proposed the use of Glycerin as a preservative for Solution of Ferrous Iodide, and in the year following, Henry Thayer (AMERICAN JOURNAL OF PHARMACY, 1858, page 390), proposed that the ferrous iodide should be prepared or formed in the presence of Glycerin. At the semi-centennial celebration of the A. Ph. A. in 1902, there was on exhibition a sample of Glycerole of Ferrous Iodide made by Prof. William Procter, Jr., January 15, 1865, and although at that time more than thirty-seven years old, it was in an excellent state of preservation. It is to be remembered that the title Liquor Ferri Iodidi in those early days was applied to an entirely different preparation from what we are now designating under the same title. The solutions of that period were much weaker and were commonly preserved with Glycerin, Honey or Sugar, and these preceded and were displaced by the formula for Syrup of Ferrous Iodide which was subsequently made official. The value of Glycerin as a preservative for ferrous salts, and likewise of iodide solutions, is now fully recognized. Its use is proposed in the pharmacopœial formulas for Diluted Hydriodic Acid and for the Syrup of Hydriodic Acid, and likewise in a number of the N. F. formulas for Elixirs containing iron salts. I have found it of value as a preservative in Iron Iodide Solutions and in the formula submitted herewith, it is used along with Hypophosphorous Acid in proper amount to render the solution permanent. In this concentrated Solution of Iron Iodide the Glycerin serves another useful purpose, namely, it prevents the crystallizing out of the salt, thus assuring solution.

The following formula is submitted for a concentrated Solution of Iron Iodide of such a strength that one volume diluted with fifteen volumes of Syrup will produce a Syrup of Ferrous Iodide practically identical in strength with the Syrup of Ferrous Iodide now official. The strength of 1 in 16 has been retained, because of its present extensive use and likewise to maintain the legal standard of much of the Solution of Iron Iodide that is already in commerce.

LIQUOR FERRI IODIDI.

Solution of Ferrous Iodide.

An aqueous solution containing 107.8 Gm. of Ferrous Iodide ($FeI_2 = 309.69$) in each 100 Cc.

Iron, in the form of fine, bright wire, cut into small pieces ..... 250. Gm.

Iodine	884. Gm.
Hypophosphorous Acid (50 per cent.)	85. Cc.
(If 30 per cent. acid be used) then use	140. Cc.
Glycerin	100. Cc.
Distilled Water, a sufficient quantity	
To make one thousand cubic centimeters.	1000. Cc.

To the Iron, contained in a flat bottom flask, add 1000 Cc. of Distilled Water, then gradually add the Iodine, keeping the temperature down by setting the flask in a vessel of cold water. When the Iodine has all been added, allow the mixture to stand for 12 hours, then heat to boiling until the clear liquid is of a bright green color. Then *cool* the solution and filter through a double filter paper and wash the flask and iron residue with several portions of Distilled Water and pass the washings through the filter. Add the Glycerin to the filtered solution and rapidly evaporate in a porcelain dish on a sand bath to about eight hundred and fifty cubic centimeters. Allow the solution to cool to 90° C., then add the Hypophosphorous Acid, mix thoroughly and when cold add sufficient Distilled Water to make one thousand cubic centimeters.

The finished product should be kept in small glass stoppered bottles entirely filled. It is an emerald green liquid, specific gravity about 1.9 (actual determination of product gave 1.906).

Syrup of Ferrous Iodide made by diluting 1 volume of this liquid with 15 volumes of Syrup (U. S. P.) showed a specific gravity of 1.35, thus practically tallying with the U. S. P. statement for specific gravity of the Syrup of Iron Iodide, and maintaining it of the International Standard of 5 per cent. of Ferrous Iodide.

In the above formula, the Hypophosphorous Acid is advisedly directed to be added to the concentrated Iodide Solution after it has been allowed to cool to 90° C. If the Hypophosphorus Acid is added to the Iron Iodide Solution before concentration, it is more or less decomposed. The Pharmacopœia states that Hypophosphorous Acid begins to decompose between 130–140° C. The decomposition appears to commence below this temperature, and in experiments where it was added to the solution before evaporation, the decomposition was quite marked. If the manipulation be changed and the Hypophosphorous Acid added before concentration, then the evaporation must be done on a water-bath.

ON THE METHOD FOR DETERMINING THE LEAD NUMBER OF ASAFETIDA.

By J. R. Rippetoe, P.D.

The "lead number" standard [1] for asafetida and its application as a test, for freedom from, or limit of foreign gum resins, in passing this drug at the ports of entry, New York in particular, has been criticised by several well known chemists (see below) but the method for determining the "lead number" does not seem to have been as closely studied.

In the spring of 1912 I had an occasion to consider this method, the particulars having been given to me by Dr. Seil of the Bureau of Chemistry, who stated at that time that asafetida had a "lead number" of 215 by the method given below, and that they were inclined to reject all importations with a number below 190. The recently published figure for asafetida is 222.[1]

In making some preliminary experiments upon selected tears of asafetida I found the values to vary as much as 66 upon the same sample. These results were called to the attention of the Government Chemists who expressed considerable surprise since they had, up to that time, never found the results to vary to any appreciable extent.

A recent abstract [2] states that the "method has been proposed as being the most accurate test showing both the quality of the gum and possible adulterants."

Five samples were examined by E. J. Parry [3] who found the "lead number" to vary from 144 to 172, and he expressed the belief that there is no authority for assuming that 220 or thereabouts represents even the approximate value of genuine asafetida.

Harrison and Self [4] examined 21 samples and found the values to vary from 18 to 250, and on repeating the determination in several cases they found a variation of 50 where a half strength lead solution was used.

The following results are given in support of my claim that the

[1] Merril and Seil, 1912 Annual Convention of the Association of Official Agricultural Chemists.

[2] *American Druggist*, Jan., 1913. 17.

[3] *Chem. and Drug.*, 1913, V. 93, p. 180.

[4] *Pharm. Journal*, Feb. 15, 1913, p. 218.

method is subject to too many variations to be relied upon for determining the "lead number" of either selected tears of asafetida or possible mixtures of asafetida and other gum resins.

The method was carried out as follows:

The alcoholic solution of the alcohol soluble matter is evaporated upon the water bath, the resin heated with water, stirring, then cooled (adding ice if resin does not separate) and the water decanted. The resin is dissolved in ether, transferred to a separator and washed with water until the water shows no turbidity. The ether solution is filtered into an exaporating dish and the solvent evaporated on the water bath. Weigh roughly about 1.1 gm. of the above resin into a tared beaker and dry for 5 hours at 110° C, cool and weigh. Dissolve in 95 per cent. alcohol and transfer to at 100 c.c. measuring flask or cylinder, care being taken that not more than 70 c.c. of alcohol is used. Add 25 c.c. of a 4 per cent. lead acetate solution, make up to mark with 95 per cent. alcohol, mix thoroughly and set aside over night. Mix thoroughly and filter thru a fluted filter; transfer 25 c.c. of the filtrate to a beaker, add 10 c.c. water and evaporate to 10 c.c. on bath; add 5 c.c. 10 per cent. sulphuric acid, and then 100 c.c. alcohol. Dissolve all separated resin and collect the $PbSO_4$ on a tared Gooch crucible, ignite and weigh.

Run a blank on the lead acetate solution and calculate milligrammes lead absorbed (weight $PbSO_4 \times 0.6830 = Pb$) by 1 gm. of the resin.

The lead acetate solution is prepared by dissolving 4 grammes lead acetate in 20 c.c. of distilled water and sufficient 95 per cent. alcohol to make 100 c.c.

The method as recently announced calls for a 5 per cent. solution of lead acetate and 80 per cent. alcohol to dissolve the resin instead of 95 per cent., otherwise it is essentially the same.

The values preceded by the letter "S" were determined by Mr. Nathan Smith to whom I am also indebted for assistance in preparation of the purified resins, etc.

Lead Number determination experiments were made upon selected samples as follows:

No. 1.—Broken asafetida tears with smooth fracture, yellowish but not pink color, 215.1, S197.3.

No. 2.—Tears yellow surface, fracture smooth, white or pink turning red 221.1, S287.0.

No.3.—Resin from No. 2 heated for 3 to 4 hour periods for

3 days continued to lose weight. Duplicate determinations of lead in the solution 291.5, S306.0.

No. 4.—Tears same as No. 2, the fracture remained white or only turned light pink 203.0, S257.0.

No. 5.—Resin from No. 4 treated same as No. 3, 296.7, S300.6.

No. 6.—Translucent tears, strong asafetida odor 70.9.

No. 7.—Resin from No. 6 treated same as No. 3, 90.2, S89.4.

No. 8.—Ammoniac tears 74.2, S80.5.

No. 9.—Tears yellow surface, fracture smooth, turning red. Four portions of the purified resin were dried and assayed as follows. The figures are duplicate determinations of the lead in the solutions:

Dried 5 hours	at 110°C.	235.3	S231.3
Dried 10 hours	at 110°C.	206.4	S207.0
Dried 20 hours	at 110°C.	221.9	S226.6
Dried 25 hours	at 110°C.	——	S201.0

No. 10.—A quantity of the purified resin used in No. 9 was dissolved in alcohol, 25 c.c. of the solution representing about 1.1 gm. transferred to a tared beaker, the alcohol evaporated and the resin dried for 5 hours at 110° C, and from this, the amount of resin calculated in the solution. The lead number of the resin dried at 110° C was determined and also 2—25 c.c. and 1—15 c.c. portions of the solution with the following results:

A	25 Cc. solution		lead number 223.5
B	25 Cc. solution		lead number 232.1
C	15 Cc. solution		lead number 250.7
D	25 Cc. solution	evaporated and dried at 110°	lead number 237.1

No. 11.—About 2½ gms. of the purified resin as used in experiment No. 9 was dried for 5 hours at 110°, cooled and weighed, dissolved in alcohol and made up to 60 c.c. 2—25 c.c. portions were assayed for lead number with the following results,—A 272.7. B 268.1.

No. 12.—A sample of purified asafetida resin prepared by Dr. Seil was examined as follows: Four assays were made. Duplicate determinations of lead in each solution were made, a, b. The crucibles were dried to constant weight at 110° C., cooled and weighed, then ignited over a Meker burner for about 5 minutes, cooled and weighed. Weights are given after drying and after ignition and lead number calculated for each.

Duplicates on blank, assay 2, after drying 0.1662 and 0.1655 gm. $PbSO_4$; after ignition 0.1603 and 0.1600 gm. Duplicate on solution

after drying 0.0863 gm. and 0.0866 gm. $PbSO_4$; after ignition 0.0809 and 0.0835 (?) gm.

Duplicates on blank, assay 3, after drying 0.2112 and 0.2111 gm. $PbSO_4$; after ignition 0.2066 and 0.2071 gm.

Assay	Resin in aliquot	Blank $PbSO_4$ Dried 110°	Ignit.	Lead No. $PbSO_4$	Dried 110° Lead No.	Lead No. $PbSO_4$	Ignit. Lead No.
1 a	0.2685	0.1842	0.1782	0.1000	214.2	0.0960	209.1
1 b	0.2685	0.1842	0.1782	0.1004	213.1	0.0952	211.1
2 a	0.2520	0.1658	0.1601	0.0864	215.4	0.0809	214.6
3 a	0.2893	0.2111	0.2068	0.1178	220.2	0.1146	217.7
3 b	0.2893	0.2111	0.2068	0.1188	217.9	0.1151	216.5
4 a	0.2408	0.2111	0.2068	0.1229	250.1	0.1194	247.9
4 b	0.2408	0.2111	0.2068	0.1239	247.3	0.1200	246.2

No. 13.—Asafetida and ammoniac tears. The purified resins of each were prepared separately and dissolved in alcohol to make solutions containing approximately 1.1 gm. in each 25 c.c. The solutions were measured into tared beakers from burettes; the alcohol evaporated upon the water bath and the resin dried in the usual manner.

ASSAYS, 11 TO 15 INCLUSIVE, WERE MADE USING A 5 PER CENT. LEAD ACETATE SOLUTION.

Assay	Resin Asafetida Soln. Cc.	Resin Ammoniac Soln. Cc.	Resin in aliquot	Blank $PbSO_4$ in aliquot dried 110° C.	Ignit.	Resin solution $PbSO_4$ in aliquot dried 110° C.	Ignit.	Lead dried 110°C.	Number ignit.
1	25	—	0.2387	0.1991	0.1961	0.1191	0.1164	228.9	228.0
2	25	—	0.2323	0.1991	0.1961	0.1118	0.1092	256.7	255.5
3	20	—	0.1916	0.1991	0.1961	0.1283	0.1261	252.8	249.5
4	—	25	0.2323	0.1991	0.1961	0.1748	0.1711	71.4	73.5
5	—	25	0.2300	0.1991	0.1961	0.1710	0.1699	83.4	77.8
6	22	3	0.2347	0.1991	0.1961	0.1217	0.1193	225.3	223.5
7	20	5	0.2329	0.1991	0.1961	0.1234	0.1212	222.0	219.6
8	20	5	0.2349	0.1991	0.1961	0.1228	0.1208	221.9	218.9
9	18	6	0.2275	0.1991	0.1961	0.1292	0.1271	209.9	207.2
10	15	10	0.2362	0.1991	0.1961	0.1340	0.1322	188.2	184.7
11	25	—	0.2355	0.2500	0.2476	0.1532	0.1520	280.7	277.3
12	25	—	0.2376	0.2500	0.2476	0.1550	0.1530	273.1	271.9
13	—	25	0.2320	0.2500	0.2476	0.2175	0.2122	95.6	104.2
14	20	5	0.2341	0.2500	0.2476	0.1655	0.1631	246.5	246.5
15	15	10	0.2352	0.2500	0.2476	0.1738	0.1723	221.3	218.7

No. 14.—Solution of asafetida resin from No. 13. Comparison of a 4 per cent. lead acetate solution with a 5 per cent. solution and

95 per cent. with 80 per cent. alcohol for solution of the dried resin. $PbSO_4$ ignited, cooled and weighed.

Assays 6 and 7.—The asafetida soln. was not dried, the resin content being calculated.

Assay	Resin Asafetida Cc.	Resin in aliquot	Lead soln. per cent.	Resin dis. in alcohol per cent.	$PbSO_4$ in aliquot Blank	$PbSO_4$ in aliquot Resin Soln.	Lead number
1	25	0.2373	4	95	0.1994	0.1112	253.9
2	25	0.2403	5	95	0.2494	0.1524	275.7
3	25	0.2373	5	80	0.2420	0.1832	169.2
4	25	0.2402	5	80	0.2420	0.1852	161.5
5	20	0.1909	5	80	0.2420	0.1877	194.3
6	25	0.2400	5	80	0.2420	0.1879	154.0
7	25	0.2400	5	95	0.2494	0.1566	264.1

The results show that the lead absorption is subject to considerable variation. Several of the factors which seem to have more or less influence are failure to obtain constant weight by drying at 110° C for five hours and the effect of the heat. The strength of the lead acetate solution and the alcohol for dissolving the dried resin are within control.

The use of 80 per cent. alcohol instead of 95 per cent. greatly reduces the absorption and the number obtained upon asafetida tears (see experiment No. 14) is much below the figure 222.

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OBSERVATIONS ON THE KEEPING PROPERTIES OF DIGITALIS AND SOME OF ITS PREPARATIONS.*

BY ROBERT A. HATCHER, M.D., AND CARY EGGLESTON, M.D.

The opinion is prevalent among both physicians and pharmacists that digitalis and its preparations undergo deterioration with considerable rapidity. Certain manufacturers have made much of this belief in the claims put forth regarding the advantages of their

* From the Laboratory of Pharmacology, Cornell University Medical College, New York City. Read before the New York Branch of the American Pharmaceutical Association, at the New York College of Pharmacy, April 14, 1913.

specialties, which, of course, are said not to be subject to such deterioration. In addition, however, to these obviously interested claims we find reports of great loss in activity of the leaf coming from men of such reputation as Focke,[1] who found deterioration amounting to 76 per cent. of the original value in two and three-fourths months in a leaf containing about 12 per cent. of moisture. He found a similar loss in one year in a leaf having 6 to 8 per cent. of moisture; leaves with 6.5 per cent. of moisture lost from 14 to 53 per cent. in strength in a year; those having 3 per cent. of moisture lost 15 per cent. in activity in the same period; and there was 5 per cent. loss in a year when the moisture had been reduced to 1.5 per cent., the low point recommended by Focke to ensure the keeping properties of the leaf.

Houghton and Hamilton[2] report their results in a series of observations upon the loss of potency of different digitalis preparations. An extract of digitalis made by percolation with fairly strong alcohol showed, on tests of eleven samples, an average loss of activity of about 40 per cent. in a period of five years—an annual loss of about 8 per cent. Eight samples of a fluid extract of digitalis, made according to the U. S. P. VII, with a menstruum of 62.5 per cent. alcohol, showed an average loss of 25 per cent. in six years—an annual loss of about 4 per cent. Eleven samples of fluid extract of digitalis made according to the U. S. P. VIII, using 48 per cent. alcohol as the menstruum, showed an average loss of 10 per cent. per year, or a total loss in activity of 35 per cent. in three and one-half years. Lastly, six samples of tincture of digitalis made according to the U. S. P. VIII showed a loss in potency of 27 per cent. in three years—an annual loss of 9 per cent. These results would seem to show that the official alcoholic fluid preparations of digitalis undergo deterioration at a rate ranging from 4 to 10 per cent. per year, varying somewhat in relation to their alcoholic content.

England[3] says of the commercial fluid extract of digitalis, "It is, largely, a concentrated hydro-alcoholic solution of certain proximate principles, or their decomposition products arising from the use of heat." He cites an observation of Roger, giving no reference, however, to the effect that a 5 per cent. maceration of

[1] *Arch. d. Pharm.*, 1903, cxli, 128.
[2] Am. Jour. Pharm., Oct., 1909.
[3] *Phil. Polyclinic*, Jan., 1897.

digitalis, when concentrated by 6.6 per cent. (*sic!*) by heat on a water bath, deteriorated to such an extent that it required sixty times as much after concentration as before to yield its toxic dose.

Hale [4] cites the observations of others on the question of deterioration, and remarks that it would seem to be fairly well established that the leaves should be dried quickly and carefully, and be properly stored so as not to become moist. Hale thus accepts Focke's views, at least to a certain extent. He does not believe, however, that it is necessary to reduce the moisture in the leaves to as low as 1.5 per cent., as suggested by Focke, and maintained by certain manufacturers who prepare a specialty along these lines. Hale reports that leaves which had been stored for eight years in a paper bag, and which contained 9.1 per cent. of moisture, gave a titre of 750 mg. per kilo of frog by the one hour method. Another sample which had been stored in a cloth bag for three years, and which contained 5.8 per cent. of moisture, required only 500 mg. to kill a kilo frog. A third specimen required 550 mg. per kilo of frog, although it contained 7.8 per cent. of moisture and had been kept in a paper bag for two years. Leaves kept in a cloth bag for a year, and having a moisture content of 9.4 per cent., also gave a frog titre of 500 mg. per kilo. By way of comparison, it may be stated that a fresh specimen of select English leaves, having 7.3 per cent. of moisture, showed 700 mg. per kilo of frog as its titre, thus: three of the old samples showed an activity greater than that of the fresh, high grade, sample of English leaves. The fourth showed an activity about equal to that of the fresh English leaf, though it had been kept in a paper bag for eight years, and in spite of the fact that it contained 9.1 per cent. of moisture.

Hale found that a sample of mouldy leaves showed a deterioration of about 90 per cent. in one year, and he cites Focke as having found that a specimen which gave a valor of 4.36 showed a valor of only 1.6 a year later, having become mouldy in the interim. It would be a useless waste of time to consider these mouldy specimens further, for, of course, they should never be used in any case.

Several observers have contended that heat caused deterioration in digitalis. Some of these are cited by Hale, who then gives some of his own observations which tend to show that temperatures below 120° C. maintained for a moderate length of time do not affect com-

[4] Hygien. Lab. Bull. No. 74, 1911.

mercial samples of the leaf. This is also borne out by the recommendation of Focke to prepare the leaf for keeping by drying it rapidly with the aid of moderate heat.

Two tinctures of digitalis, made with 70 per cent. alcohol, in Hale's hands showed a frog titre after eight years which was equal to that of the average fresh tincture prepared from a high grade new specimen of English leaf. On the other hand, assays of a number of digitalis preparations obtained in the open market showed a little deterioration in twenty-two months. Three samples of official fluid extract lost 4.3, 6.9, and 8.7 per cent. respectively in this time. Four non-official preparations, obtained at the same time and under like conditions, showed deterioration from 14.3 to 33.3 per cent. in the same interval of time.

Moran [5] records a number of observations, which include some contradictory results, made upon different samples of tinctures of the same age; thus, one showed no deterioration in four years, while another is stated to have appeared "to have deteriorated considerably," in the same time. He also tested a tincture which was twenty-four years old and one made from an extract which was nineteen years old. In the case of both of these he says that the activity was probably due to the saponin present, inferring that they retained no digitalis action at all. In the meagre details that he gives, however, he states that the perfusion of 20.0 c.c. of the twenty-four year old specimen through the heart of a frog caused, "No tonic effect, acceleration of beat; systolic arrest." Of the tincture from the nineteen year old extract only 11.0 c.c. were required to give "No tonic effect; no slowing; systolic arrest." When the tincture which had not deteriorated was used slowing and tonic effect were observed and systolic arrest was caused by 12.0 c.c. It is true that the typical digitalis action on the frog's heart is early slowing with the so-called 'tonic effect,' and systolic arrest is the typical end reaction. However it is not infrequent to see a heart poisoned with digitalis react atypically with no slowing, or even with acceleration, and in any case the stage of slowing is usually soon followed by one of acceleration. It is quite possible that Moran's frogs happened to react atypically, or that the stage of slowing was brief and overlooked, the heart passing into that of acceleration. Clark [6] perfused frog's hearts with digitonin, the

[5] *Medical Chronicle*, No. 55, 1911–1912, p. 1.
[6] *Brit. Med. Jour.*, 1912, II, p. 687.

saponin body of digitalis, and found that, while it caused "systolic effect," its action was, ". . . produced instantaneously, but is not complete, the auricles and part of the ventricles continuing to beat for some hours." Further, he found that in the concentration of 0.01 mg. per c.c. of Ringer's solution it has no action, while the action described above is produced when the concentration is raised to 0.1 mg. per c.c. of fluid. It is probable that the results reported by Moran were not due to saponin alone, for it is doubtful if this substance is present in the tincture in sufficient concentration to have any effect on the heart such as that described. This is supported by Kiliani,[7] who states that there are but the merest traces of digitonin in digitalis. Certain it is that the end reaction of systolic arrest is a typical digitalis action, and is not what Moran terms a "saponin effect." If we consider, as we are almost compelled to do, that the systolic arrest seen by Moran was due to digitalis action and not to saponin, then his twenty-four year old tincture still possessed 60 per cent. of the activity of his undeteriorated tincture, and the nineteen year old extract showed no deterioration.

Moran's own conclusions are to the effect that a tincture should retain its activity for two or three years, but it is difficult to interpret Moran's results.

Goodall,[8] in a note on the keeping properties of the tincture of digitalis concludes that the "tincture of digitalis probably retains its full activity for one year, but that after that period deterioration of its potency to an important extent is likely to take place." His experiments are not given in detail, hence it is impossible to determine the exact value which is to be placed upon his findings, particularly as the information given suggests certain decided defects of technic and control.

Haynes (cited by Goodall without reference) is stated to have found that tincture of digitalis would keep for two years without material change in activity. He kept his specimens in the dark.

We have cited sufficient evidence to show the trend of opinion, and it may be mentioned that the pharmacopeias of several countries, namely, the French, Swiss, and German, require that the supplies of digitalis leaf be renewed annually. The German pharmacopœia has adopted the recommendations of Focke to the effect that the leaf should be dried over calcined lime and kept in small,

[7] *Arch. der Pharm.*, ccxliii, p. 7.
[8] *Brit. Med. Jour.*, I, 1912, p. 887.

completely filled glass containers, protected from light and moisture.

In spite of the general consensus of opinion to the effect that age, moisture, light, and heat, alone or variously combined, according to the observer, cause marked and rapid deterioration in digitalis leaves and alcoholic fluid preparations, we long since came to a contrary opinion, for we had observed that samples of powdered leaf which had been in the laboratory in cardboard containers for several years, and tinctures prepared from these leaves at different times in the past few years, retained their activity almost, if not quite, unimpaired. Stimulated by this apparent anomaly, we undertook an investigation of the question of deterioration of digitalis leaf and some of its preparations.

We began by making new tests of the activity of our own old samples of the leaf and of tinctures made therefrom. Comparing the results of these tests with the records of previous ones, we found that none of the specimens which were four or five years old showed any material deterioration. These samples of leaf and tincture had been kept without any special care, the tinctures being stored in glass-stoppered bottles and exposed to the light and temperature changes of the laboratory. The leaf, as has been mentioned, was kept in the original cardboard containers, and not protected in any way from either heat or moisture changes as these occurred in the atmosphere of the laboratory, but it should be said that the storeroom is unusually dry for this climate. The cat method was employed for the estimation of the activity of the specimens, and in some few instances we also used the one hour frog method with results quite in accord with those obtained with the cat. We sought to obtain some older specimens than ours, and, through the courtesy of E. R. Squibb & Sons, and Gilpin, Langdon & Company, we were supplied with samples of the leaf, ground and unground, tinctures, extracts, and fluid extracts ranging from less than one to more than thirty years old. With some of these we conducted tests on both cats and frogs.

A sample of German digitalis which had been kept in paper for three years on a jobber's shelf was received in the form of No. 60 powder and was found to contain 7.5 per cent. of moisture. It gave a cat unit of 110 mg. per kilo of cat weight. A sample of English leaf in fine powder, which had been kept on a shelf in paper for three years, gave a cat unit of 128 mg., and it contained 6 per cent. of moisture. Both of these were considered by the jobbers

as being entirely worthless except as specimens. The fallacy of this view is obvious, for each was found to have an activity about equal to that of the average fresh specimen of good quality. By the cat method the average unit for digitalis, in terms of leaf, is 100 mg. per kilo of cat weight; the range of variation in activity of different fresh specimens of good quality runs from 75 mg., for the most active samples, to 120 mg. for the less active. Since these two showed no deterioration we then examined the oldest specimen of leaf which we had obtained.

This was a sample of about 12 gm. of whole dried leaf which had been kept in a glass-stoppered bottle for not less than twenty-five years. The entire specimen was powdered and passed through a No. 60 sieve. After thorough mixing, 10 gm. of this powder were extracted as follows: The powder was moistened with 4.0 c.c. of dilute alcohol (U. S. P.) and allowed to stand for twenty-four hours in a cylindrical percolator; it was then packed tightly and percolation was started; this was allowed to continue until about 30.0 c.c. were obtained; percolation was then interrupted, maceration continuing until the following day, when percolation was again allowed to proceed until 100.0 c.c. had been obtained.

Three tests by the cat method gave the following units: 74 mg., 95 mg., and 82 mg., an average cat unit of 87 mg. per kilo. Perfectly fresh samples of the most active leaf which we have been able to procure have not shown a lower cat unit than 65 mg. per kilo. This twenty-five year old leaf was, therefore, of very high activity, better even than the average fresh specimen. The leaf was very dry and, although we did not determine its moisture content, we may assume, according to the statements of Focke,[1] that it contained much more than his required minimum of 1.5 per cent., especially as the specimen had not been preserved with any particular care. This specimen, therefore, had almost certainly undergone no deterioration during twenty-five years of standing.

The cat has been said, incorrectly we believe,[9] to be unsuitable for the detection of deterioration owing to the toxic nature of the products of such deterioration, but none of our cats showed atypical effects.

We also examined this specimen by the one hour frog method, and found the fatal dose to lie between 900 and 1000 milligrams

[9] Amer. Jour. Pharm., lxxxv, 1913, p. 99.

per kilo of frog, which is about 25 per cent. higher than the average as determined by Hale, and by Famulener and Lyons.[10]

It is probable, however, that the results obtained by the cat method are the more nearly correct in this case, for it is well known that frogs vary considerably in susceptibility to the digitalis bodies, such differences have been discussed fully in the article previously cited,[9] and we would refer the reader to that for confirmation of the statement.

Turning to the fluid preparations, we found that a sample of the fluid extract made over ten years ago gave a cat unit of 110 milligrams of leaf per kilo. This specimen was made with 50 per cent. alcohol as the menstruum, and probably showed no deterioration.

A sample of fluid extract of digitalis which was said to be "not less than thirty years old" was then tested on the cat, three tests giving units of 130, 162, and 153 milligrams per kilo respectively, an average cat unit of 148 milligrams, the action being perfectly typical of digitalis. As we have no means of knowing the original activity of the leaf from which this fluid extract was made we might assume that it was of the average strength, that is, that it would originally have shown a unit of about 100 milligrams. On this basis we might suppose that in more than thirty years it had declined only about 40 per cent. in activity. As a matter of fact, it was more active by 32 per cent. than the average of thirteen specimens of fluid extract obtained in commerce in the present year, the explanation being that it is especially difficult to prepare a fluid extract of digitalis which represents the full activity of the leaf.

This thirty-year-old fluid extract having been made according to the Pharmacopœia of 1870, had a menstruum composed of about 70 per cent. alcohol, 20 per cent. glycerin, and 10 per cent. water. Tests of this specimen by the one-hour frog method gave a fatal dose of about 1300 milligrams per kilo of frog. This is almost certainly too high a figure, and may be attributable to the presence of glycerin in the preparation. Glycerin often delays absorption from the lymph-sac of the frog and makes the specimen which contains it seem weaker than it actually is,[9] but this is without influence in the case of tests made on the cat by our method.

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[10] Proc. Am. Pharm. Association, L, 1902, p. 415.

This specimen of fluid extract of digitalis had, therefore, probably undergone no deterioration in thirty years, since, as stated, it was far more active than the average *fluid extract* of digitalis now in use.

England [3] contends that heat, even when moderate and applied for a comparatively short time, causes enormous loss of activity in the fluid preparations of digitalis. Focke controverts this statement by the results of his experience in the concentration by heat on the water bath of aqueous infusions of digitalis when they are too weak to be tested on the frog. He recommends concentration by 50 per cent. and finds that the process causes no reduction in activity. In this country nearly all of those who use the frog method of standardizing digitalis preparations employ heat to reduce the amount of the alcohol before testing such preparations as the tincture.

To these statements with regard to the influence of heat we may add that we found a sample of solid extract of digitalis, which was made in 1908, and which was said to represent two and one-half times the weight of leaf, to have a cat unit of 52 mg. per kilo (that is, 128 mg. of the leaf). There was no obvious loss in activity, although the preparation had been reduced to the consistency of a solid extract by means of evaporation in the presence of heat.

At this point we decided to stop further testing of the dried leaf and of those pharmacopœial preparations of digitalis made with a menstruum containing 50 per cent. or more of alcohol, for it was evident that deterioration does not occur to any considerable degree in such forms of the drug, under ordinary conditions.

It is unnecessary to mention the infusion further than to state that frequent observations confirm the well known fact that it is prone to undergo rapid deterioration even in the presence of a small amount of alcohol, such as is now used.

Deterioration of digitalis in the presence of water is further well illustrated by the following experience: We diluted a tincture of digitalis of known strength with nine parts of normal saline solution and set it aside, closely stoppered, for seventeen days. It was exposed to the light during this time, and for the most part was in an unheated room, though on some days it was exposed to a temperature of 70° F. for as much as five hours at a time. On the seventeenth day after dilution we tested this solution on cats and

found a unit of 81.5 mg. of leaf per kilo. (Three tests, 84.6, 71.0 and 89.0 mg. per kilo respectively). On the same day we tested the tincture from which the dilution had been made and found it to have a cat unit of 62.2 mg. of leaf per kilo (two tests, 61.8 and 62.7 mg. respectively). In a period of seventeen days, then, this aqueous dilution of a tincture of digitalis had lost 31 per cent. of its original activity. It is remarkable that it had not lost more than this, and the low temperature of the room may be partly responsible for its comparatively moderate deterioration.

The deterioration of aqueous preparations of digitalis has long been recognized and this fact has recently been recalled by Cushny,[11] who says of strophanthus, squill and digitalis that " Their active principles readily undergo decomposition when the tincture is diluted with water. . . ."

We are disposed to remark that it is irrational to dispense the tincture of digitalis already diluted with water, or with an aqueous vehicle. The physician should order the necessary dilution to be made by the patient each time that he takes the prescribed dose, or should employ a vehicle containing a sufficient amount of alcohol.

There is one other preparation which deserves notice, only to be condemned. This is the acetic fluid extract. A sample of this preparation which was made in 1901 was found to be practically without digitalis action. In order to avoid the disturbing influence of the acetic acid present in the specimen 5.0 c.c. were neutralized with an excess of sodium bicarbonate and evaporated on the water bath to a soft extract. This was treated several times, while still on the water bath, with strong alcohol; the alcoholic extract was decanted and evaporated. It was then taken up with 5.0 c.c. of diluted alcohol, making a clear solution. This was further diluted with normal salt solution to make 50.0 c.c. This solution was then tested on a cat in the usual way. At the end of an hour the animal had received a quantity which represented 1000 mg. of digitalis leaf per kilo. As the animal showed no perceptible effect save slight slowing of the heart (due, in all probability to the fluid injected), it was released. Five hours later it had still shown no positive digitalis effect.

This same preparation—acetic fluid extract—was injected into

[11] *Brit. Med. Jour.*, 1912, II, p. 685.

the ventral lymph sac of each of three frogs. The first weighed 14.5 gm. and received 0.25 c.c. total, the second 21.0 gm. and received 0.5 c.c. total, and the third weighed 21.5 gm. and was injected with 1.0 c.c., an amount equal to about 5000 mg. per kilo of frog. None of the frogs died.

A second sample of acetic fluid extract of digitalis was tested to see if a fresh preparation was active. This sample was made on January 16, 1913, and was tested on the 29th of the same month, only thirteen days after its preparation. It was found to have a cat unit of 925 mg. per kilo, or, roughly, it had only about 10 per cent. of its supposed activity.

From the foregoing it is obvious that this preparation is worthless. This is only what is to be expected, for the decomposition of glucosides by dilute acids is universally recognized.

In addition to these tests of the leaf and galenical preparations we have tested some of the proprietaries with reference to their deterioration. One of these, which has been claimed to be permanent, namely Digalen (liquid), gave the following results:

Two specimens obtained in 1912 were tested at the same time and one gave a cat unit of 1.52 c.c. per kilo, while the other gave a unit of 2.45 c.c. per kilo. A specimen obtained in 1908, and kept sealed as originally sent out, gave a cat unit of approximately 3.0 c.c. per kilo when tested in November, 1912. In the case of the first two specimens, obtained fresh at the same time, the stronger was almost 100 per cent. more active than the weaker. The specimen of 1908 was only about half as active as the one of 1912. It is fair to assume that all of the batches of digalen are originally made of the same activity, and if this assumption be correct this preparation is subject to far more rapid deterioration than either the digitalis leaf or its galenical preparations, which contain 50 per cent. or over of alcohol. The examples cited are but representative of our results with many different specimens of digalen.

It remains for us to discuss briefly some of the opposed findings here recorded.

All whose observations have been cited used frogs exclusively as the test animals in their determinations. Cloetta has contended that fresh digitalis contains little or no digitoxin, but that this constituent is developed during storage. It is known that digitoxin is irregularly and relatively slowly absorbed from the lymph spaces of the frog. If Cloetta's contention is correct the development of

digitoxin during keeping would have a tendency to make the drug appear to have undergone deterioration when tested on the frog. On the other hand, such a change would not materially affect the activity of the drug when tested by the cat method, for in this the factor of absorption is entirely eliminated. The statement of Focke that it is in the first few weeks after harvest that digitalis deteriorates most rapidly, and to the greatest extent, exactly coincides with the explanation just offered.

Conclusions.

1. Commercial digitalis leaves of good quality do not undergo any deterioration in many instances as the result of age; in a few cases they do appear to have deteriorated, but only with extreme slowness—at a rate probably not exceeding 1½ to 2 per cent. a year.

2. The same statement holds for the Pharmacopœial preparations made with a menstruum containing at least 50 per cent. of alcohol.

3. Heat below 120° C., applied for a reasonable length of time, does not cause deterioration in digitalis leaves, aqueous infusions, or alcoholic preparations; in the latter case even though the preparation be reduced to a soft solid.

4. The acetic fluid extract of digitalis is worthless.

5. Liquid Digalen is decidedly inferior to the alcohol-containing galenical preparations of digitalis in so far as permanency is concerned.

DIGITALIS. FOXGLOVE.[1]

Common Name: Foxglove, Purple Foxglove.[2]

By John Uri Lloyd, Phar.M.

Digitalis frequents silicious lands, but does not thrive in limestone soil. It is native to, but unequally distributed, over such localities as the Madeira Islands, Portugal, Spain, France, Ger-

[1] Part of a treatise on Digitalis in the Lloyd Laboratory Series, published in advance.

[2] The term *Digitalis purpurea* is not precise. The earliest references cite that its flowers range from white to purple, and it is a matter of regret that the name is not characteristic.

many, and especially England. It is widely cultivated, not only for its medicinal properties, but also as a garden flower, being well

Fig. 1. Flower and fruits of Digitalis. (Much reduced.)

known under the common term Foxglove, a name ascribed to it both from its resemblance to an ancient musical instrument known as Foxes Glen, and from its fancied resemblance to a gloved finger.

Tragus was "the first systematic author who noticed it, and from him it received its name, Digitalis (from digitus, finger), in allusion to the German name Fingerhut, signifying a finger-stall, the blossoms resembling the finger of a glove."—*Withering.* (See blossom, Fig. 1.) The home of the most prized Digitalis is England.

Fig. 2. Digitalis bed in the author's garden, Cincinnati, Ohio. (Much reduced.)

Digitalis is easily grown in lands and countries fitted to its culture, reproducing from self-sown seed. Motherby (1775) states that "it grows only in gravelly beds," a statement that has been carried through subsequent literature, but is not fact, although we accept that the plant "prefers" such soil. In limestone lands Digitalis failed, under our personal observation, to respond satisfactorily to cultivation. Limestone sections of Kentucky, although very fertile otherwise, and producing luxuriant crops of corn and heavy

tobacco, failed utterly with Digitalis, although an abundance of seed of unquestioned fertility was employed. In gardens, however, in limestone sections of both Kentucky and Ohio, the transplanted plants thrive for two seasons, but the seeds therefrom fail to maintain the crop. (Fig. 2.) In New York State, in the valley of the Honeoye River, Digitalis planted in 1820 in a flower garden on the homestead of the Webster family (the home of the writer's mother) at the present date (1912) continues as a great wild bed, self-sown from year to year.[3] In some parts of the State of Oregon, Digitalis, escaped from cultivation, has become a thick roadside plant, growing near Cloverdale luxuriantly and in such abundance as to have led to its consideration as a commercial crop. To Dr. Walter F. Brown, of that city, we are indebted for nice specimens of the leaf, and photographs showing the flower-spikes over nine feet high.[4] He writes as follows:

> Replying to your questions I will say:
>
> 1. As near as I can find, Digitalis has been growing here for twenty years. It was confined to a few spots for several years, but it is now found all over the southern half of this county.
>
> 2. It is supposed to have been brought here by pioneers, and cultivated for its flowers.
>
> 3. The dairymen claim that some cows will eat it in early spring, when the leaves are tender and other forage is scarce. It has no noticeable effect on the animals that eat it, but they eat very little of it.
>
> 4. I have used the infusion and the tincture for about fifteen years, and of late years I have used digitalin to some extent.
>
> 5. People in this locality make no use of the plant, but look upon it as a despicable weed that takes their hillside pastures.

Other than the high price of labor in this country, there is no reason why Digitalis should not be American cultivated, and produce in abundance sufficient to supply all our needs, from localities such as Oregon, suited to its growth.

Part Used. The leaf of the second year's growth is generally directed by "authority" to be used, but in our opinion this limitation to the second year's crop is ill-advised and unnecessary. The mature leaves of either the first or the second year's crop (Fig. 3)

[3] M. I. Wilbert, of Washington, D. C., informs us that under favorable circumstances Digitalis may become a perennial. Possibly this is a factor in its luxuriant growth in the localities mentioned.

[4] We regret much that these photographs were too faint for half-tone reproduction.

are superior to immature or overripe leaves of any year. The standard of excellence should be the fully-matured, air-dried leaf, regardless of the age of the plant, and we question if collectors anywhere discriminate concerning the age of the plant. In this connection we would state that, originally, both the root and the

Fig. 3. Prime Digitalis, second year, in flower and seed. (Much reduced.)

leaf of Digitalis were employed in medicine. The root, however, is exceedingly variable in structure, that of the first year's growth being insignificant and sappy, whilst the root of the second year's growth is larger and heavier, and more pronounced in quality. Inasmuch as the leaf possesses fully the qualities of the drug, and is more easily collected, it naturally displaced the root in medicine. Thus the preference once given to the second year's growth of the

root created both the confusion and the prejudice whereby the *leaf of the first year* was finally ostracized, even in authoritative literature. Thus both Pharmacopœias and standard works on materia medica were illogically led to exclude much excellent Digitalis material. In searching for data in this direction, we find that Withering, in 1785, writes as follows:[5]

Fig. 4. Matured leaves of Digitalis, first year growth, much reduced.

My truly valuable and respectable friend, Dr. Ash, informed me that Dr. Cawley, then principal of Brazen Nose College, Oxford, had been cured of a Hydrops Pectoris by an *empirical exhibition of the root* of the Foxglove, after some of the first physicians of the age had declared they could do no more for him. I was now determined to pursue my former ideas more vigorously than before, but was too well aware of the uncertainty which must attend on the exhibition of the *root* of a *biennial* plant, and therefore continued to use the *leaves.*

In connection with the leaf-selection, Withering is also explicit in distinguishing between the qualities of the leaves gathered at *different seasons of the year,* but he does not limit the drug to

[5] From "*An Account of the Foxglove,*" by William Withering, M.D., Physician to the General Hospital at Birmingham, London, 1785.

the second year's growth. Upon the contrary, he states that at different seasons of the year the quality varies greatly, which, we will remark, is true of all herbs. He therefore restricts the leaves employed to those of a *prime quality, gathered when the plant is in flower,*[6] making no other reference whatever to either the first or the second year's crop. We quote as follows:

"These[7] I had found to vary much as to dose, at different seasons of the year; but I expected, if gathered always in one condition of the plant, viz., when it was in flowering state, and carefully dried, that the dose might be ascertained as exactly as that of any other medicine; nor have I been disappointed in this expectation."

During the past fifteen years the writer has cultivated more or less Digitalis, but has failed to discover any advantage that the second year's crop possesses over the mature leaf of the first year, other than that there is a greater number of mature leaf of the second year, the crop being heavier than the first year. In the original European experimentation the seed and flowers were also employed in therapy, but soon passed into disuse.[8] Withering employed the leaf texture (Fig. 5) after removing the ribs and fibers.

Constituents.

So energetic a drug as Digitalis became, naturally, an early prey to the interstructural desecrater and the reckless destroyer of natural substances. To the many products created and evolved, seemingly every conceivable play has been made on the name of the drug. Some of these names have been applied and reapplied to materials so different from each other as to lead to hopeless con-

[6] The second year is the flowering year.—L.

[7] The leaves.—L.

[8] When assayed by the Keller-Fromme method, the radical leaves of Digitalis yield from 0.527 to 0.531 per cent. of digitoxin, the flowers from 0.563 to 0.585 per cent., and the seeds from 0.215 to 0.225 per cent. A. Barenstein (*Pharm. Zeit.*, 1910, 56, 128). Hirohashi (*Jour. pharm soc.*, Japan), on the contrary, concludes as follows: 1. The small upper leaves of the plant are more active than the large middle and lower leaves. 2. The leaves should be gathered before budding sets in. 3. The flowers seem to contain a larger amount of the active principles than the leaves. 4. The flowers retain their activity for a year, red and white being identical. 5. The seeds are physiologically as active as the leaves and flowers. The stems are poorer in active principles.—*Drugg. Cir.*, Feb., 1913.

fusion. Some have been affixed to mixtures of educts, and others to products of manipulation so different, in our opinion, from any natural constituent of Digitalis as to lead one to wonder how the

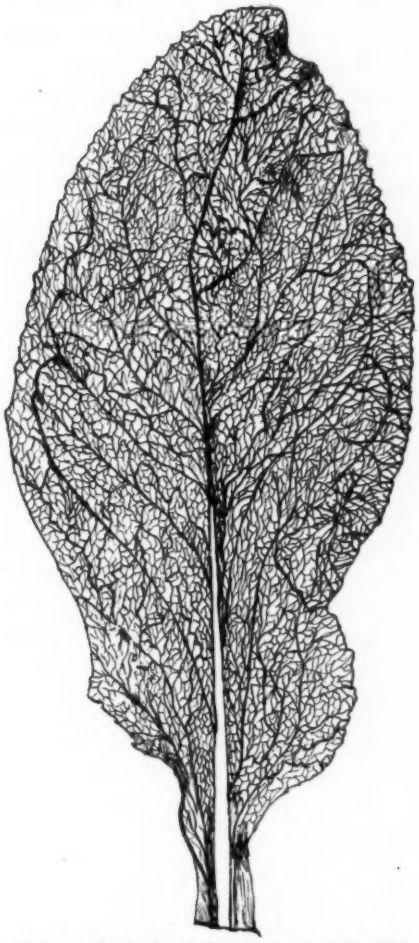

Fig. 5. Digitalis leaf, pen drawing by Miss Eda Van Guelpen, showing texture and ribs. Much reduced.

plant would view itself, could it know that its tortured flesh had given rise to such a grotesque litter of abnormal, misnamed creations.

Up to the eighteenth century nothing of consequence chemically

had been applied to the drug. Thompson, in his *London Dispensatory,* 1811, p. 419, alludes to the fact that Destouches established inorganic compounds of calcium and potassium, whilst Radig found potassium acetate.[9] Thompson also made a personal examination, establishing "a deep-green resinous matter, in which its narcotic power resides." Leroyer, of Geneva, afterward gave the names *Digitaline* and *Digitalia*[10] to a material made by a circuitous chemical process, in which it is questionable whether the final product had any place in the original drug. After discussions, Thompson sums it up as "an extractive mixture," adding that "the active principle of Digitalis is unknown."

Came then Walz (1846–1858), Kosmann (1845–1860), Homolle and Quevenne (1845–1861), Nativelle[11] (1872), Schmiedeberg (1874), the last of whom made a most exhaustive research.[12]

From that date to the present, thousands of chemists have sought the secrets of Digitalis, all ignoring the natural combinations of organics and inorganics, all seeking a toxic agent as the desirable therapeutic constituent, and all, so far as we can discover, believing that agent to be *organic* only.[13] Seemingly in it all, natural associations of textural relationship of the organic and inorganic are ignored. First destroy the natural substance of the drug, then from it create anew, is the idealistic process, which needs no other comment than that, after more than one hundred years of these aggressive destructive methods by the most brilliant chemists, the verdict is by many persons accepted, as by Thompson, in 1811, "still unknown."[14]

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[9] The time will come, in our opinion, when such as these will become of great interest. The *inorganic* side of *organic* life is not to be lightly passed over.

[10] The terminations *ine* and *ia* were both once used as alkaloidal affixes. See "The Eclectic Alkaloids," etc., Lloyd Library Bulletin, No. 12.

[11] For this research the Orfila prize of 6,000 francs was awarded, in 1872.

[12] See *Pharm. Journ.,* V, 1875, abstract by Flückiger.

[13] Likewise the cathartic principle of Senna and Rhubarb becomes largely elusive to the destructive chemist. The agricultural chemist has learned the importance of inorganics in plant foods, so in a time to come must chemists in other directions. The study of *textures* embracing the natural inorganic compounds is yet to become a promising field.

[14] From time to time enthusiastic searchers have rested their labors on a supposed triumph that, under the touch of others, has proved elusive. Even now not one but several believe the cry is answered by some Digitalis fragment that will influence the heart of a beast.

Accepting our own inadequacy in the attempt to untangle this knot, and our own dilemma in this labyrinth of threads, we arranged with Professor Dr. H. Kiliani, of Freiburg, Germany, than whom there is perhaps no better living authority on Digitalis, to contribute succinctly to this treatise, under his own name, the present standing of the fairly established Digitalis products and educts. This we now present, believing it to be the latest word on the Digitalis constituents, products, and educts.[15]

Chemistry of Digitalis Purpurea.

By Professor Dr. H. Kiliani, Freiburg, Germany.

In a critical study of the more important digitalins of commerce (1874), Schmiedeberg (*Arch. f. experim. Path.*, vol. 3, p. 16) arrived at the conclusion that these preparations were composed mainly of the following principles: *Digitonin, digitoxin, digitalin,* and *digitalëin,* the first a secondary matter, the three others acting upon the heart, *digitoxin* possessing this property in a most prominent degree. My own researches have extended the knowledge of the chemical nature of these substances.

Digitonin I found easily crystallizable from 85 per cent. alcohol, and it can be extracted by means of this solvent from water-soluble, commercial seeds-digitalin. When crystallized, digitonin is less soluble in water than when amorphous; its solution foams when shaken. It is little soluble in alcohol, insoluble in ether, chloroform, and benzin, and forms an insoluble tannate. The more recent researches yield the formula $C_{54}H_{92}O_{28}$, or $C_{55}H_{94}O_{28}$; warmed with diluted hydrochloric acid, digitonin splits into *digitogenin,* $C_{30}H_{48}O_6$, or $C_{31}H_{50}O_6$,[16] and four molecules of hexose (galactose and dextrose).[17] Digitonin is inert upon the heart, but as a "saponin"—substance acting hæmolytic; this action is annulled by addition of cholesterin (Ranson, *Deutsche mediz. Wochenschr.*, 1901, p. 194), the latter forming the inactive compound *digitonin-cholesterid* (Windaus, *Ber. d. d. chem. Ges.*, vol. 42, p. 238; 1909).—*Schmiedeberg's digitonin* was a *mixture*[18] of the just described substance with another completely amorphous "saponin."

[15] This contribution was made some months ago. Possibly, were the article now at his command, the author might revise it somewhat.

[16] Ber. d. d. chem. Ges., Vol. 32, p. 2201 (1899).

[17] Ibid. Vol. 24, p. 341 (1891).

[18] Arch. d. Pharm., Vol. 243, p. 5 (1905).

Digitoxin, $C_{34}H_{54}O_{11}$,[19] easily crystallizable, is insoluble in water (when free of other digitalis glucosids or extractive matters); it dissolves freely in alcohol and chloroform, slightly in ether, and is insoluble in petroleum ether (Keller, 1897). Schmiedeberg could not establish the presence of sugar as a constituent of digitoxin; he obtained only the amorphous toxiresin by the action of acids. I resolved digitoxin into crystallized *digitoxigenin,* $C_{22}H_{32}O_4$, and two molecules of easily crystallizable sugar, $C_6H_{12}O_4$, *digitoxose.*[20] *Nativelle's digitalin* and *Arnaud's digitaline cristallisée* are probably identical with digitoxin.

Digitalin (characteristic granules, very little soluble in water, insoluble in ether, chloroform, freely dissolving in alcohol). Schmiedeberg proved this to be a glucosid, but he obtained as product of hydrolysis only a resinous substance (digitali-resin). I established the digitalin to be a uniform substance, $C_{35}H_{56}O_{14}$, notwithstanding its refusal to crystallize, and I resolved the pure "*digitalinum verum*" into well crystallized *digitaligenin,* $C_{22}H_{32}O_3$, or $C_{22}H_{30}O_3$, dextrose and digitalose, $C_7H_{14}O_5$.

Digitalëin.—At first I had questioned the existence of this substance as an individual body, but later researches proved without doubt that the seeds *and* the leaves contain a considerable quantity of an easily water-soluble substance, vigorously acting upon the heart; yet all endeavors to isolate that very decomposable matter in pure condition have thus far proved fruitless.

Cloëtta's *digalen* (like many another similar digitalis-product) contains certainly a high percentage of digitalëin, but it is not proved to be a uniform substance, and Cloëtta's claim of having transformed it into *digitoxin* and vice versa, is surely erroneous.

Tests for Digitoxin, Digitalinum verum and Digitonin.—Keller's test for digitoxin: Dissolve the substance in glacial acetic acid containing a little ferric chloride; float this solution upon strong sulphuric acid; at the line of contact appears a dark zone, and after a few minutes the acetic acid liquor becomes dark blue (indicating in this way 1/10 of a milligramme of digitoxin in 1 Cc. of acetic acid). This test is more sure and can also serve for *digitalinum verum,* and (negatively) for *digitonin;* when used in the form

[19] Ber. d. d. chem. Ges., Vol. 31, p. 2457 (1898).

[20] For constitution see: Ibid. Vol. 38, p. 4040 (1905).

proposed by me; 100 Cc. of pure, strong sulphuric acid; and, on the other hand, 100 Cc. of glacial acetic acid are mixed each with 1 Cc. of a solution of 5 g. of ferric sulphate in 100 Cc. of water. Several tenths of a milligramme of the material to be examined are dissolved in 3–4 Cc. of the glacial acetic acid containing ferrum, and beneath this is allowed to flow an equal volume of the aforementioned sulphuric acid: *Digitoxin* acts as in the test of Keller (dark *blue* in the acetic acid), because containing digitoxose; *digitalinum verum,* on the other hand, colors the *sulphuric acid* yellow, afterwards red, and finally *red-violet,* resembling the flower of digitalis. Pure *digitonin,* applied in the same small quantity, causes *no kind of color.*

Keller's method of determining the amount of digitoxin in the leaves, produces, according to experiments of Windaus and the author, doubtful values, the product not being uniform.

The *older literature* contains the description of many substances as *digitalosmin, digitasolin, paradigitaligetin* and others, which were surely amorphous *mixtures.*

Medical History.

Digitalis has been used in domestic medicine from the earliest date, and has been employed for numerous affections that are more or less connected with heart disturbances. The recording of the titles alone of the works of past authorities in medicine, concerning this drug, would require pages. We shall therefore select a few only of these writings that, for our purpose, are most important.

Rayser (chemist and druggist) is authority for the statement that the term "*Foxes glofe*" occurs in the Saxon Herbarium, 1000 A.D., and again under the name *Cerotheca vulpis,* in a manuscript of the fourteenth century titled *Sinonama Bartholimei.*[21]

Welsh physicians[22] as early as 1233 commended Digitalis in

[21] *Chemist and Druggist,* London, X Rayser ii.

[22] *Physicians of Myddvai.* The domestic physician of Rhys GRYG, prince of South Wales, who died 1233, made a collection of recipes used in medicine, at that date in his country. He was assisted by his three sons, the collection being a valuable historical record concerning remedial agents and methods of that date. Of this, two compilations have been issued, the two appearing together, 1861, with a translation by John Pughe (470 pp.). The original manuscript is in the British Museum.

ointment form and in decoction, while both Fuchs (*Fuchsium*) [23] and Tragus,[24] 1552, figured the plant beautifully and gave it much attention, the former introducing the name *Digitalis.* (See page 216.) Boerhaave (*Historical Plants*) considered Digitalis too acrid or poisonous for internal use, whilst Alston, of Edinburgh, says, "Though this herb is not now in use, it is almost of as great efficacy as any drug the Indies produce." The *Catalogue of Plants,* by Caspar Schvvenckfelt, 1600, describes Digitalis as a drug in which the *flowers,* used in decoction as a gargle, subdue fever and inflammation, while the *leaves* relieve bowel troubles.

Between this period and 1785 the works on domestic medicine, as well as the English dispensatories, gave passing attention to Digitalis, the comments, however, being largely repetitions of each other, and all being copied from earlier publications. The following, from Salmon's *New London Dispensatory,* 1632, may be cited as typical of the then prevailing opinion concerning the ascribed qualities of the remedy:

> *Fox-Glove, Hot and Dry.* It is bitter, cleansing, opening, cutting and attenuating: It expectorates thick flegm, if drunk with Mead, takes away obstructions of the Liver and Spleen, is an extraordinary good wound-herb, prevalent against the King's evil, and may be used instead of Gentian. Two handfuls of the herb taken with Polypody ℥iiij. helps the Epilepsy.—*Salmon's New Dispensatory,* London, 1600.

In 1783 Digitalis was made official in the Edinburgh Pharmacopœia, "in consequence of the recommendation of Dr. Hope," although Rayser (*Chemist and Druggist,* 1910), states that it had

[23] Leonhard Fuchs was a Bavarian, born in Membdingen, 1501. In 1524 he graduated in medicine, became involved in religious controversies by reason of becoming a Protestant, was made Professor of Medicine in Tübingen, 1535, and died in 1566. The Lloyd Library contains his publications, as follows: De Stirpium, in the following editions:

1545, Latin edition.
1549, French edition.
1551, Latin edition.
1558, French edition.
1673, French edition.

[24] Hieronymus Bock, known in literature as *Tragus,* was born at Heiderbach, in the Zweibrucken, 1498. Instead of becoming a monk, as was intended, he became a Protestant, then a schoolmaster, and finally a preacher. He practiced medicine and wrote on Botany. The Lloyd Library has his *De Historia Stirpium,* 1552.

received Pharmacopœial recognition elsewhere as early as 1650. Concerning the 1783 Pharmacopœia, Withering says:

> From this, I am satisfied, it will be again very soon rejected, if it should continue to be exhibited in the unrestrained manner in which it has heretofore been used at Edinburgh, and in the enormous doses in which it is now directed in London.

Came, in 1785, the monumental work of 206 pages, by William Withering, M.D.,[25] who, in the following passage, gives to local empiricism the credit of having excited his interest in this remedy:

> In the year 1775, my opinion was asked concerning a family receipt for the cure of the dropsy. I was told that it had long been kept a secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed. I was informed, also, that the effects produced were violent vomiting and purging; for the diuretic effects seemed to have been overlooked. This medicine was composed of twenty or more different herbs; but it was not very difficult for one conversant in these subjects, to perceive that the active herb could be no other than the Foxglove.

In the Preface to his book, Withering states his reason for the effort as follows:

> The use of the Foxglove is getting abroad, and it is better the world should derive some instruction, however imperfect, than that the lives of men should be hazarded by its unguarded exhibition, or that a medicine of so much efficacy should be condemned and rejected as dangerous and unmanageable.

This antedated the hypodermic syringe as well as the physiological experimenter, but yet Withering intrudes on animal experimentation, for he introduces a description of the experimental action of Digitalis leaves upon a turkey fed with the drug, concluding as follows:

> At length he refused all nourishment. On the fifth or sixth day the excrements became as white as chalk; afterwards yellow, greenish, and black. On the eighteenth day he died, greatly reduced in flesh, for he now weighed only three pounds.
>
> On opening him we found the heart, the lungs, the liver and gall-bladder

[25] *An Account of the Foxglove and Some of its Medical Uses,* with Practical Remarks on Dropsy and Other Diseases, by William Withering, M.D., Physician to the General Hospital at Birmingham. Published in London, 1785.

shrunk and dried up; the stomach was quite empty, but not deprived of its villous coat.—*Hist. de l'Academ.*, 1748, p. 84.

In those days of heroic medication it was naturally concluded that a drug that could thus kill a turkey must be a good medicine to cure a human being, a process of reasoning not yet altogether obsolete.

After much discussion with his professional friends, Withering records his opening experiences, as follows:

> In the summer of the year 1776, I ordered a quantity of the leaves to be dried, and as it then became possible to ascertain its doses, it was gradually adopted by the medical practitioners in the circle of my acquaintance.

Having stated that the cases he cites were "proven from my own experience," Withering closes his historical Preface by the admirable and conservative summing up of the whole matter as follows:

> After all, in spite of opinion, prejudice, or error, time will fix the real value upon this discovery, and determine whether I have imposed upon myself and others, or contributed to the benefit of science and mankind.

Between 1776 and 1785 the Digitalis discussion became very pronounced, and even acrimonious. The entire English medical profession became more or less involved, some considering the drug too poisonous to use, but the majority pushing it to the limit, and lauding its therapeutic qualities.

BOOK REVIEWS.

THE QUALITATIVE ANALYSIS OF MEDICINAL PREPARATIONS. By H. C. Fuller, B.S., Chief Analyst of Institute of Industrial Research, Washington, D. C. First Edition. First Thousand. John Wiley & Sons, N. Y. 12 mo.—vi+132 pages. Cloth $1.50 net.

The almost unlimited possibilities in the matter of composition of medicinal preparations makes it a difficult task to attempt to outline any systematic procedure for the recognition of the hundreds of active principles of drugs, of which a number may be present in the same preparation. Mr. Fuller, the author of the book whose title is given above, has had abundant experience in the line of examination of such preparations to qualify him for the task which he has attempted, but it is to be regretted that the usefulness of the

work will be somewhat curtailed by the evident incompleteness and haste with which it has been prepared for publication. There is a mass of valuable material which will prove useful to every analyst who has to meet such problems as this book is intended to aid in solving if he will take the time to thoroughly go over the detailed scheme of separation and key the various starting points of new subdivisions in the text, to agree with the synopsis of the scheme as given on page ix.

It is also a matter of regret that the author did not think it necessary to warn the analyst who follows the scheme, of the unreliability of color reactions (p. 45, etc.), when several alkaloids may be present, nor to mention the fact that tannin is often extracted from acid solutions by petroleum ether and ether in amounts sufficient to obscure color reactions for small amounts of other principles.

The chapter (or section rather, for the book is confusingly run together without chapter or section headings) on resins is very unsatisfactory from the standpoint of an analyst who wants advice regarding their identication and it is hardly the place in a book of this character to quote so extensively from the work of Powers and Rogerson on the subject of jalap resin, for the information given is of no practical use whatever.

The directions for the preparation of the aurochlorides of the solanum bases (p. 57) is scarcely a practical procedure on account of the smallness of the amount of such bases usually found in a medicine. The table of melting points of these aurochlorides, however, belongs here and not on page 76, where it is inserted under the resins, an unrelated subject.

Opposite page 78 is a table which on page 79 is described as giving the color reactions of cocaine and other local anesthetics. Strangely enough, while the reactions of the other local anesthetics are given in detail, cocaine is altogether missing.

The detailed directions for the treatment of some of the classes of preparations are rather disappointing. Under Emulsions on page 88 the advice to "examine the gummy residue on the filter" will hardly bring joy to the heart of the analyst who arrives at this stage of the work. Under Toothwashes, a list of numerous probable ingredients is mentioned, but saccharin, which is frequently used as a combined sweetener and antiseptic, is overlooked and under the Dusting Powders, zinc stearate, a frequent constituent, is also omitted.

On page 78 it would be advisable to suggest the use of the microscope in connection with the examination of this insoluble residue, for many mineral as well as animal and vegetable substances can be positively identified only by this means.

No provision is made at any place in the scheme for the recognition of peroxides or perborates, which would be overlooked if the plan were followed literally and it is surprising that no reference is made to the separation and identification of paraphenylene diamine, frequently found in hair dyes.

Typographically, the book shows the same carelessness or haste in preparation. Subheadings are evidently omitted in the lists of substances on pages 2 to 12, although found in later lists. There is a strange omission of alkaloids from the preliminary lists mentioned above, although they appear in their proper place in the detailed scheme beginning on page 36.

On page 22 " test " is used for "taste " and on page 88 " ether " is used for " aqueous solution." On page 12 "fluorescence " is twice misspelled although correctly spelled on the following page.

The use of the reformed spelling by which the final " e " of alkaloids is omitted is regrettable. There is a lack of uniformity also in this matter, as apomorphine is spelled both with and without the final " e " on pages 52 and 54, and aspidosamine, page 56 (which, by the way, appears neither in the preliminary list nor in the index) carries the final " e."

The system of italicizing all substances which are likely to be commonly met with should have been done uniformly throughout the book and should have been done with greater care. For instance, on page 20 the items picric acid and pyrogallol are italicized while in the same list the substances phenolphthalein, resorcinol and ichthyol, all of which are found with equal or greater frequency, are not so emphasized.

The book is one which will be very useful to such analysts as have had experience in this line of work and it is to be hoped that future editions will find it greatly improved as it is pioneer work along a line which deserves greater attention than it has heretofore had. Dr. Fuller is to be congratulated upon his having taken the initiative and produced a work which will largely replace the obsolete Dragendorff as the hand-book of the analyst of medicines.

C. H. LaWall.

FOOD INSPECTION AND ANALYSIS. By Albert E. Leach. Third Edition Revised and Enlarged by Andrew L. Winton. New York: John Wiley & Sons. London: Chapman & Hall, Limited. 1913. $7.50.

With the passage of the Food and Drugs Act in 1906 it was necessary that public analyst, health officers, sanitary chemists and food economists should have a work on the standards of purity of food products, with approved methods of analysis. It was fortunate not only for the government but for the manufacturers of food products that already in 1904 the first edition of Leach's work was published.

Without entering into detail as to the contents of this work we may say that it is very complete and true to the title a work on "Food Inspection and Analysis." The present edition has been revised and enlarged and contains new matter equivalent to about 80 pages, not including some 40 pages changed in the last thousand of the second edition, and 12 new cuts, have been added. The size of the work, however, has been increased but 47 pages, some of the earlier matter being replaced by new, thus performing a double service to the reader.

Among the new features are improved general methods and apparatus for the determination of moisture, ash, and arsenic, modern apparatus for the Babcock test, processes for the detection of foreign fat in dairy products, methods for the determination of ammonia and acidity in meat, and of sugars in cereal products, correction of Munson and Walker's sugar table, new methods for vinegar analysis (including glycerine determination), schemes for the separation of food colors, a subchapter on formic acid (recently introduced as a preservative), methods for the analysis of lemon and orange oils, a summary of analyses of authentic samples of vanilla extract, and a complete revision of the final chapter on fruit and vegetable products with new sections on tomato ketchup, dried fruits, preserves (including maraschino cherries), fruit juices, and non-alcoholic carbonated beverages. In the final chapter are included descriptions of recent methods for the determination of tin, vegetable acids, and habit-forming drugs, and for the detection of saponin, also microscopical methods for the detection of spoilage.

The text of the Federal Pure Food Law, as amended during the present year, and of the Meat Inspection Law, are added for ready reference as an Appendix.

The substantial work of T. B. Osborne in the subchapter on proteins and of W. D. Bigelow in the chapter on meats, both introduced in the second edition, appear unchanged in the present edition.

The author has been fortunate in having associated with him Dr. Kate Barber Winton, whose services in the revision are acknowledged by the author. This new edition of "Leach-Winton," as it will probably come to be known, will be found indispensable to analysts.

THE PLANT ALKALOIDS. By Thomas A. Henry, Superintendent of Laboratories, Scientific and Technical Department, Imperial Institute. Philadelphia: P. Blakiston's Son & Co. 1913. $5.00 net.

All accurate studies upon the active principles of medicinal plants are of interest to pharmacists. The last word, as to the proper menstruum to be used in the manufacture of medicinal preparations and the proper method of procedure to be followed, will not have been said until the important constituents have been isolated and experimented with both chemically and physiologically.

Several good books have already been published upon the plant alkaloids. In Dr. Henry's book we find that he has pretty well digested the original communications upon the study of alkaloidal drugs in both England and the United States as shown by the references to the original literature. This has, however, not been done at the expense of the work of continental investigators, whose researches receive their share of attention. The assay methods are also included and very many reactions for the detection of alkaloids are also given. The physiological action of many of the principles is given, no doubt, because of the interest at the present time in biological assays.

ALLEN'S COMMERCIAL ORGANIC ANALYSIS. Vol. VII. Vegetable Alkaloids, Glucosides, Non-Glucosidal Bitter Principles, Animal Bases, Animal Acids, Lactic Acid, Cyanogen and its Derivatives. Edited by W. A. Davis and Samuel S. Sadtler. Philadelphia: P. Blakiston's Son & Co. 1913. $5.00 net.

The new edition of Allen's Organic Analysis which has been entirely rewritten is a veritable mine of information for pharmacists. While of course these volumes primarily appeal to chemists and manufacturing pharmacists, yet they contain just the information that

the retail pharmacist very often is in need of. As with the preceding volumes so in the present volumes there are a number of eminent contributors. Dr. G. Barger, of London, has written the monographs upon "Vegetable Alkaloids" and "Ptomaines or Putrefaction Bases"; Dr. E. Frankland Armstrong, of Reading, England, contributes the chapter on "Glucosides"; Mr. G. C. Jones, of London, is the responsible editor for the article on "Non-Glucosidal Bitter Principles"; Dr. A. E. Taylor, of Philadelphia, has written the monograph on "Animal Bases"; Dr. J. A. Mandel, of New York City, is the author of the article on "Animal Acids"; Mr. Davis, of Harpenden, England, has written the monograph upon "Lactic Acid"; and the final chapter upon "Cyanogen and its Derivatives" represents the work of Mr. Herbert Philipp, Perth Amboy, New Jersey.

The text is illustrated with drawings of several of the substances occurring in a crystalline condition. This portion of the work might well be extended although it is likely that chemists usually pay very little attention to the forms of crystals of pure substances. The references to the literature of original articles is quite extended and for all practical purposes will be found to be sufficient. Some of the articles are very complete and likely to be of very great service at the present time. The article on " lecithins," and in fact the whole chapter on "animal bases" has been presented particularly well. Owing to the interest in lactic acid and its derivatives this chapter also is likely to be frequently consulted and the information applied practically.

CHLORIDE OF LIME IN SANITATION. By Albert H. Hooker. New York: John Wiley & Sons, 1913.

As has been already pointed out in this JOURNAL (1905, vol. 77, pp. 265-281; 1906, vol. 78, pp. 140-144) emergency methods for the purification of drinking water, as (when contamination is beyond control), are very much needed. Such methods are likely to be of a more or less chemical nature. Chlorine has lately been largely advocated and is quite extensively used. The present book contains a vast amount of information on the use of chloride of lime in sanitation. There are also more than 400 abstracts of important articles with references to the original literature.

WILLIAM McINTYRE, PH.G.; PH.M.[1]

William McIntyre was born in 1843 in the North of Ireland. He was brought to this country by his parents when he was a small boy. His family settled in the district of Kensington, the north-eastern section of Philadelphia. Here he lived with the family and attended the public schools, passing the various grades and entering the High School which he attended faithfully for three years. At the end of this time he entered the pharmacy of John Bley to begin his career as a pharmacist. Mr. Bley had a system of testing the honesty of the boys he took into his store, but it did not take him long to find out that William McIntyre was above and beyond any temptation to do a dishonest act.

In 1861 he matriculated in the Philadelphia College of Pharmacy. This was during the Civil War and with a desire to serve his country, he enlisted in a Pennsylvania Regiment, but, being a minor, he was prevented from carrying out his patriotic intentions by the opposition of his father, who thought that he was entirely too young. He graduated from the College in 1863. The class at that time was very small, consisting of only twenty-two members. After his graduation, he entered business on his own account on Frankford Avenue. He was filled with the ideals of the professors at the College—Procter, Bridges, Parrish, and Maisch—and he carried out their principles in his daily work. Nothing that would cater to vice and immorality could be purchased in his store.

He inherited in large measure the character and virility which distinguished the sterling Scotch-Irish people who have given so many able men and women to the world.

In 1867 he joined the American Pharmaceutical Association which met in New York City that year; he was a life member of this Organization and contributed many valuable papers and reports. In 1881 he joined the Pennsylvania Pharmaceutical Association and soon became well-known and greatly appreciated by all of its members and in 1893 he was elected president of this body. He was also a member of the Philadelphia College of Pharmacy and became one of the Board of Trustees. In the pharmaceutical meetings of the College he took an active part and was its Secretary

[1] Read at Annual Meeting of Philadelphia College of Pharmacy, March 31, 1913.

for many years. The reports of the meetings were extensively published not only in this country but abroad.

In 1906 he helped to organize the Philadelphia Branch of the American Pharmaceutical Association and became its president in 1908. He was elected treasurer of this body and continued to hold this position until the time of his death. The Philadelphia Association of Retail Druggists was organized in 1899 with Mr. McIntyre as president. He held this office until 1901.

Notwithstanding his busy life as a pharmacist, he took a great interest in children and their education and in 1876 he was elected a school director, devoting a large part of his time to improving conditions and advancing the interest and comfort of both teachers and scholars. Both came to him with their troubles, sure of sympathetic advice and counsel. He entered into minute details to further serve them and when a window was broken, a gate out of order, or a furnace leaking coal-gas, he saw to it that repairs were made without delay. Such devotion extending over a long period of years brought recognition and he became a member of the Board of Education, being reappointed as his term expired, the last being for the long term under the new law governing schools in Philadelphia.

Thirty-seven of his years were given to pharmacy, and when he retired from business, while giving the greater part of his interest to the Board of Education, he retained his love and interest in Pharmacy. After retiring from business he removed from Kensington to his late home at 2434 N. 32nd Street. He was president of the Kensington Electric Company, for years assisted in the organization of the Frankford Avenue Business Men's Association, and took an interest in many other charitable and fraternal organizations.

William McIntyre believed thoroughly in the principle "Mens sana in corpore sano." "Mac," as he was lovingly called by his friends, was always willing to join in athletic exercises and he was often found with the younger men ready for almost any physical exercise which they proposed. He enjoyed swimming, bicycling, and walking and in the pathetic incidents of his last walk when his strength gave out and he was forced to stop by the wayside, the true fiber of the man was revealed in his thoughtful words to those who came to his assistance, when he asked them not to tell his wife in order that she might be spared from the shock.

William McIntyre passed away beloved by all. His life is one continuous reminder to those of us who remain to make the best

of our abilities with the keynote ringing through life by giving the best service possible to others ungrudgingly and springing from no other motive but love.

EDWIN M. BORING,
JOSEPH P. REMINGTON,
WILLIAM L. CLIFFE.

PHILADELPHIA COLLEGE OF PHARMACY,

ANNUAL MEETING.

The Annual Meeting of the Philadelphia College of Pharmacy was held March 31st, 1913, at 4 P.M., in the Library. Twenty-two members were present. The minutes of the quarterly meeting, held December 30th, 1912, were read and approved. The minutes of the Board of Trustees for December, 1912, January and February, 1913, were read by the Registrar, J. S. Beetem, and approved.

The annual meeting is the time when the President and the other Officers and Committees submit annual reports. Abstracts from these reports are as follows:

President's Report: The College buildings are in good condition, various repairs having been made during the year, among which may be mentioned that carbon lamps have been replaced by Tungsten lamps. A number of improvements were made in the Pharmaceutical Laboratory giving increased facilities for class and individual instruction. Several analytical balances were placed in this laboratory for the estimations of alcohol in galenical preparations, and other operations requiring accurate weighing.

The total number of students in attendance at the present time is 420, a large number from the different classes are either taking special courses or are doing special work in connection with their theses.

In the analytical chemistry course and microscopical course a large number of the students are doing special work.

A number of inquiries have been received for the names of graduates who could be recommended to fill special positions where a thorough training in chemistry was a requisite requirement. And with the continued enactment of laws for the protection of our citizens the demand for graduates in pharmacy, who are familiar with pure food and drug requirements, will largely increase.

The hot house and roof garden continues to demonstrate its usefulness in making it possible to conduct numerous experiments with most beneficial results.

During the year four active and three associate members were elected. Six active members have died, viz., Clemmons R. Parrish, Henry Mueller, M.D., Miss Florence Yaple, Alexander H. Jones, William McIntyre, and Horace W. Estlack.

Obituary reports of some of the above have been published in the AMERICAN JOURNAL OF PHARMACY, and of the others memoirs will be presented at the June meeting.

Committee on Pharmaceutical Meetings: Since the last Annual Meeting Pharmaceutical Meetings were held in April and May. At the meeting in May a recorder was elected as provided by the by-laws. There has been a growing lack of interest in these meetings by the retail pharmacist notwithstanding the efforts put forth to make attractive programs. A special meeting of the committee was called to consider the advisability of discontinuing the meetings. The committee decided to suspend the meetings till the beginning of the new year, as it is strongly believed that interest in the meetings will sooner or later be revived, but it is very necessary if this is to be accomplished to have an active recorder who can attend to the meetings and prepare suitable programs.

Publication Committee: The AMERICAN JOURNAL OF PHARMACY has been published regularly during the year. All bills for the year have been paid. The unusual balance is mainly due to increased sale of back numbers, which indicates a healthy interest in the Journal. An inventory was taken during the year of all of the volumes of the American Journal of Pharmacy in stock. During the past year there has been received by gifts from Adam Pfromm & Co. some 50 volumes of the Journal, the oldest being 1848.

Editor's Report: During the past year there has been published 570 pages—exclusive of an 11-page index—making an average of 47½ pages to an issue. This matter included 65 original and selected papers covering a wide range of subjects relating to pharmacy

As the editor of a pharmaceutical publication naturally the articles which have to do with the manufacture of pharmaceutical preparations appeal to him as being of paramount importance. During the past year we were fortunate in having from our own members a number of articles which reflect credit upon the College and Journal, of these the following articles may be mentioned: A

Note on Tinct. Cardamoni Compositæ, by John K. Thum; Lime Water, by Herbert J. Watson; Liquor Sodii Phosphatis Comp., by Mitchell Berstein; Notes on Elixir Ferri Quiniæ et Strychnia Phosphatis, and an improved formula, by W. L. Cliffe; Kieselguhr, by Henry C. Blair; Rhubarb as a Source of Color in place of Golden Seal, by John K. Thum; and the articles by George M. Beringer on Purified Charcoal, and on Cudbear as a pharmaceutical coloring. In looking over the remaining papers it is also interesting to note that very many of them are contributions from either members of our College or graduates of the same.

Curator's Report: The collection in the museum are growing, especially the specimens of historical interest.

Additional shelf room is needed for their accommodation and display. The museum needs, also, the systematic work of some one who is able to give his entire time to the work and build up the collections. The museum contains a wide range of rare and valuable drugs, and it should be kept up to date, and open all the time, so as to be available for consultation and study every day.

Librarian's Report: Not many books have been added to the Library by purchase during the year. The donations were 116 volumes. A total of 4863 books are now ready to be catalogued. A number of periodicals and theses were bound. We receive through the government the Census Reports, Treasury Reports, Reports of the Library of Congress, Smithsonian Institution, Public Health, and Commission of Labor Reports, Daily Consular Trade Reports, and Bulletins and Circulars of the Department of Agriculture. A number of American, English, and German Journals are subscribed for, and a number are received through the exchange list of the AMERICAN JOURNAL OF PHARMACY and the *College Bulletin*. The Library has been used by 873 persons during the year.

Mr. E. M. Boring, for the committee appointed to draft resolutions and prepare a memoir of our late fellow member, William McIntyre, submitted their report, which was on motion referred to the Publication Committee, for insertion in the AMERICAN JOURNAL OF PHARMACY (see p. 234).

Committee on Necrology reported they had received a memoir of the late Charles S. Braddock, of Haddonfield, N. J. And also of the late Alexander H. Jones, which were on motion also referred to the Publication Committee.

A letter was received from Doctor T. F. Hanausek, of Wien,

acknowledging the receipt of his notice of election to honorary membership.

Donations were received from Mr. William A. Keeney of a card containing the labels of some of the older druggists of the city, dating back as far as 1846. Also a bill containing items of drugs made out by Thomas Penn in 1740. And from William M. Morrison, several horn cups for syrup bottles, believed to be about 75 years old. The thanks of the College were tendered the donors.

The President made the following appointments:

Committee on By-Laws: George M. Beringer, Joseph W. England, C. A. Weidemann.

Delegates to Pennsylvania Pharmaceutical Association: C. B. Lowe, Joseph P. Remington, F. P. Stroup, O. W. Osterlund, Henry C. Blair, William E. Lee, E. M. Boring, Charles H. LaWall, James C. Perry, W. A. Rumsey.

Delegates to New Jersey Pharmaceutical Association: George M. Beringer, Henry Kraemer, C. B. Lowe, H. L. Stiles, H. P. Thorn.

The Committee on Legislation, to fill vacancy, Richard H. Lackey.

Annual Election: Messrs. W. A. Rumsey and Mitchell Bernstein were appointed tellers.

The Secretary, was, on motion, directed to cast an affirmative ballot for those offices where there was no contest. After a ballot was taken the tellers reported the result of the election, when the chair announced that the following were elected:

President, Howard B. French; 1st Vice-President, R. V. Mattison, M.D.; 2nd Vice-President, Joseph L. Lemberger; Treasurer, Richard M. Shoemaker; Corresponding Secretary, A. W. Miller, M.D.; Recording Secretary, C. A. Weidemann, M. D.; Curator, Joseph W. England; Editor, Henry Kraemer, and Librarian, Katharine E. Nagle.

Trustees: S. P. Sadtler, W. L. Cliffe, and H. K. Mulford.

Publication Committee: Samuel P. Sadtler, Henry Kraemer, Joseph W. England, Joseph P. Remington, Martin I. Wilbert, Charles H. LaWall, and John K. Thum.

Committee of Pharmaceutical Meetings: Henry Kraemer, Joseph P. Remington, C. B. Lowe, M.D., George B. Weidemann, and E. M. Boring.

C. A. WEIDEMANN, M.D.,
Recording Secretary.

ABSTRACT FROM MINUTES OF THE BOARD OF TRUSTEES.

December 3rd, 1912. Eighteen members were present. Professor Moerk present by invitation. Committee on Library reported that a number of additions had been made to the Library by gift and purchase. Seventy-six persons had consulted the Library. Committee on Instruction reported a very important matter relating tc educational interests, a general discussion ensued, resulting in the appointment of a Special Committee of Three to draft a suitable letter and resolutions to be reported at a subsequent meeting of the Board. Committee on Finance presented a report which was, on motion, adopted.

December 6th, 1912. Fourteen members were present. Professor Moerk present by invitation. The Special Committee to whom had been referred the educational matters under consideration made their report and same was discussed by Messrs. French, Sadtler, England and Beringer, and finally adopted. Mr. Beringer referred to our method of advertising the College, and moved that the entire matter of advertising be referred to the Committee on Finance and Committee on Announcement; it was so ordered. Professor Remington stated that a friend of the College had presented to the institution four water coolers and would supply the drinking water free of charge and moved that a vote of thanks be tendered the donor; so ordered.

January 7th, 1913. Ten members were present. Committee on Property stated that the present lighting plant was barely able to meet the demand. The Committee had obtained an estimate for installing Tungsten lamps in place of the Carbon ones in use; thereby reducing the required power and producing a more satisfactory light. The committee was authorized to make the change. Committee on Examinations reported that the names of five gentlemen upon whom they recommended that the Honorary degree of Master in Pharmacy be conferred at the next commencement. In accordance with the By-laws, the names were referred to a special committee of three and the Chair appointed R. M. Shoemaker, Howard B. French and C. A. Weidemann.

February 4th, 1913. Eighteen members were present. Committee on Instruction reported that several meetings of the Committee had been held and the subject of changing the course fully discussed, the conclusion being that a change at this time was not desirable. The educational matters that had been under discussion

at the December meeting were again considered and freely discussed by Messrs. Beringer, French, Remington, Mattison and England. A sub-committee of three was appointed to consider some features of the subject that had not been decided and to make report at a subsequent meeting. Professor Sadtler on behalf of the Joint Committee to whom had been referred the subject of advertising the College, proposed a plan for consideration. This was discussed by Messrs. Mattison, Lee, Leedom, Beringer and England and on motion adopted. Professor Remington referred to the death of William McIntyre, and moved that a Committee of Three be appointed to take proper action. This was agreed to, and the Chair appointed Messrs. Boring, Cliffe and Remington. Propositions for membership were received from two persons, which on motion, were referred to the Committee on Membership.

February 24th, 1913. Sixteen members were present. The Special Committee to whom was referred the names of five gentlemen recommended for the Honorary degree of Master in Pharmacy, reported in favor of their election. A ballot was taken and they were unanimously elected. Committee on Scholarship had no special report, but a letter was read from Doctor R. V. Mattison relative to the action of the Board in making the Keasby and Mattison Scholarship perpetual. The Special Committee of Three on educational matters presented, for consideration and discussion, additional subjects that would probably require legislative action during the present session. As a matter of interest the Dean announced that Doctor John Uri Lloyd would be in the city the day following, and asked that as many members as possible meet him at the Drug Club. Mr. French read a communication from Dr. W. P. Wilson inviting members of the College or any of the Classes to visit the Commercial Museum. The communication was referred to the Dean to bring to the attention of the students, and if possible arrange for a visit.

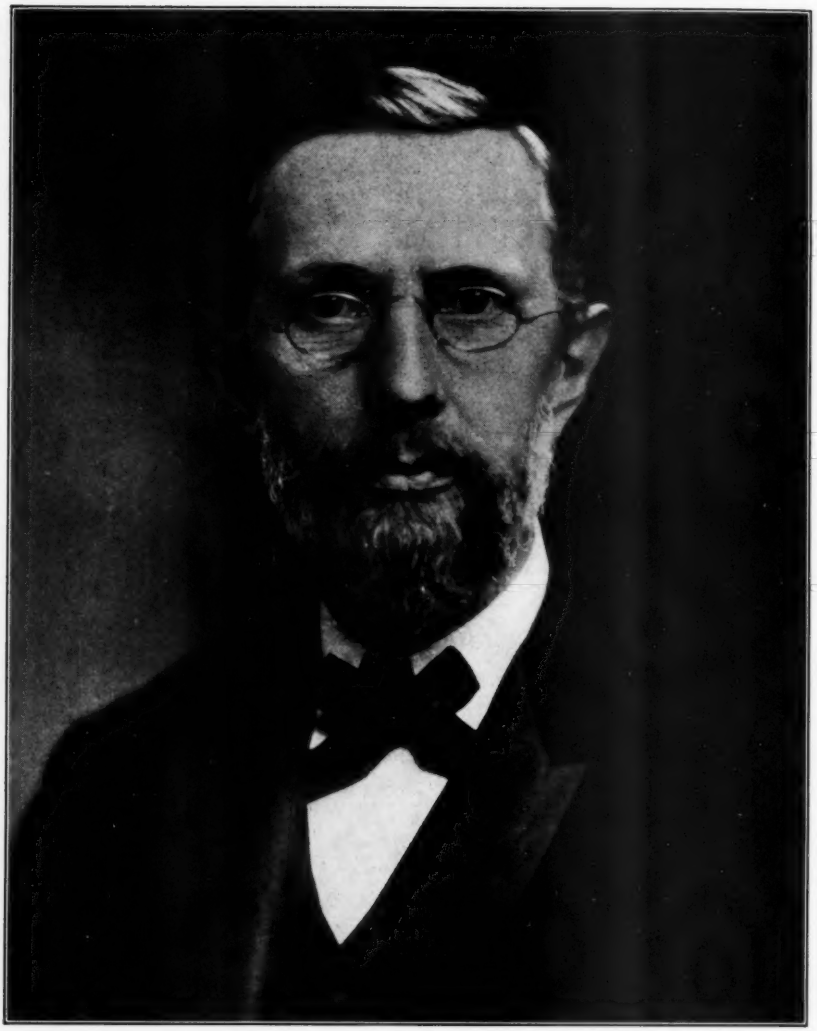
PHARMACOGNOSY OF CUBEB.

In the abstract published last month (pp. 193, 194) concerning "The Oil from Spurious Cubebs" a very interesting portion was omitted through lack of space. Mr. J. C. Umney was curious to see why the Amsterdam oil had such an extraordinarily low optical rotation and after having procured some of the Amsterdam cubebs

from which the oil was derived submitted them to his assistant, Mr. H. V. Potter. They were subsequently very thoroughly studied by E. M. Holmes, Curator of the Museum Department, Pharmaceutical Society of Great Britain, who found that they were a very mixed lot. In fact he found in the specimens submitted, similar fruits to those which he had already described on May 2, 1885 (*Pharm. Jour.*, **3**, xv, p. 909) as being admixed with a lot of genuine cubebs examined by him at that time. These spurious fruits possess a mace-like odor, do *not* give a crimson coloration with sulphuric acid and indeed possess poisonous properties. It was due to the presence of these spurious fruits that the Amsterdam oil, referred to, owed its low optical properties. These spurious fruits were at one time supposed to be derived from *Piper crassipes*. They have since been referred to as a variety, *Rinæ badak*. In all probability they are a distinct species, differing in both odor and structure of the fruit, from any of the *Piper Cubebas*. While classed as a Cubeb by the Java Dutch, they nevertheless recognize it as distinct. The genuine cubebs *Piper Cubeba* var. *Rinæ Katoentjar* and the larger stalked *Piper Cubeba* var. *Rinæ tjaloeroek*, are easily distinguished by the fact that they give a crimson coloration upon the addition of sulphuric acid while the spurious article, *Piper Cubeba* var. *Rinæ badak* does not.

Mr. Holmes has contributed a number of valuable papers during the past 25 years upon the pharmacognosy and commerce of cubebs. A complete summary of his work with that of other investigators (who, in many instances, have been supplied with material by him) is published in the *Pharmaceutical Journal* **88**, 1912, p. 604. This work has been very painstaking and ought to interest pharmacists, general wholesale dealers, and brokers in particular. It should be mentioned that there are two other recent articles on cubebs by Mr. Holmes which should be consulted, viz., those published in the *Perfumery and Essential Oil Record*, **3** (1912) p. 64 and **5** (1912) p. 125.

Owing to the confusion among writers of textbooks, as seen by their illustrations of cubeb fruits, Mr. Holmes prevailed upon Mr. J. Small to make a comparative study of different fruits in the herbarium and museum of the Pharmaceutical Society of Great Britain. He then examined a number of commercial samples. Out of five commercial samples, four proved to be heavily adulterated with fruits of *P. C.* var. *Rinæ badak* (*Pharm. Jour.* **88**, 1912, p. 639).



OSCAR OLDBERG, 1846–1913.